REMARKS

Election/Restriction

Applicants confirm the elected species discussed in the Office Action with traverse. The traversal is on the ground that the Patent Office has not established that it would pose an undue burden to examine the full scope of the claimed invention.

Claim Rejections under 35 USC §§ 101 and 112, second paragraph

The claims are amended to overcome the outstanding formality issues. The claims are not narrowed.

With respect to the allegation that it is unclear what is the meaning of "m>1" in the definition of 17a, applicants point to the $C_nF_mH_o$ group in the definition of R^{17a}. Thus, meaning that there are more than 1 F atoms in the group $C_nF_mH_o$.

Claim Rejections under 35 USC § 112, first paragraph

Claims 10-13 were rejected as allegedly not enabled. The subject matter of claims 10-12 and of suitable dependent claims are now in new claims 14-17. Claims 14-17 are directed to a method of treatment and claim 13 is directed to a pharmaceutical composition.

Applicants respectfully disagree with the rejections.

With respect to claim 13, the pharmaceutical composition claim, the invention that one skilled in the art must be enabled to make and use is that defined by the claims. Claim 13 is directed to a pharmaceutical composition comprising a compound of an enabled claim and a pharmaceutically acceptable adjuvant and/or vehicle. The rejected claim is thus a dependent composition claim, dependent on an enabled independent compound claim. There is no apparent reason why a composition comprising an allowed and enabled compound and a conventional pharmaceutically acceptable adjuvant and/or vehicle would not be enabled. If a compound is enabled, a composition comprising said compound and a pharmaceutically acceptable adjuvant and/or vehicle must by definition be also enabled, as pharmaceutically acceptable adjuvants and/or vehicles are well known in the art.

The Examiner by making the rejection appears to treat the composition claim as if it was a method claim directed to a specific use, i.e., a pharmaceutical application, i.e., administration to humans. However, applicants are not required to enable a method of treatment when a composition is claimed. Applicants must enable what is claimed. Here a composition is claimed, therefore a composition is what needs to be enabled. The composition claim is not limited to a specified use as a method claim may be. The compositions may be used for any purpose, including, e.g., the in vitro aspects taught in the specification or in vivo ones and others.

The Federal Circuit has specifically held that a composition claim cannot be read to embrace only certain uses because the composition claim would otherwise mutate into a method claim. See *Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 54 USPQ2d 1227 (Fed. Cir. 2000), wherein the Federal Circuit stated that "the '393 patent claims compositions of matter. The scope of these composition claims cannot ... embrace only certain uses of that composition. ... Otherwise these composition claims would mutate into method claims. The district court correctly applied this principle, refusing to narrow the scope of the claimed compositions to specific uses." Accordingly, composition claims should not be treated as if they were method claims. A composition therefore comprising an enabled compound and a conventional pharmaceutically acceptable adjuvant and/or vehicle must also be found enabled.

With respect to the enablement rejection over the method of treatment claims, first and foremost, a specification disclosure which "contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Marzocchi*, 169 U.S.P.Q. 367, 369 (1971). "The PTO must have adequate support for its challenge to the credibility of applicant's statements of utility". (The quoted statement was made in the context of enablement, i.e., the how-to-use requirement of the first paragraph of section 112.) See also *In re Bundy*, 209 USPQ 48 (1981). The only relevant concern of the Patent Office should be over the truth of assertions relating to enablement. The first paragraph of section 112 requires nothing more than objective enablement. See *In re Marzocchi, supra.*

The Examiner has not established any basis to doubt objective enablement. The Examiner has also provided no support for establishing that one of ordinary skill would doubt the objective truth of the asserted utility, which is enabled by the specification. The enablement rejections by the Examiner are thus unfounded. The rejection therefore was improper under *In re Marzocchi.*

The claims rejected are directed to the treatment of an androgen-dependent diseases and to the treatment of prostate cancer, the treatment of which are not objectively doubtable. Doubt has been held reasonable only where, for example, the invention has been characterized as "highly unusual," *In re Houghton*, 433 F.2d 820 (CCPA 1970), as "incredible," *In re Citron*, 325 F.2d 248, (CCPA 1963), or as "too speculative," *In re Eltgroth*, 419 F.2d 918 (CCPA 1970). Because compounds having similar therapeutic activities are known in the art, the existence of a new class of compounds having the claimed activities is not objectively doubtable, i.e., not "highly unusual," "incredible," and/or "too speculative."

The specification teaches that "known antiandrogens, which are already used in clinical practice for prostate cancer treatment, are CPA (Schering AG), flutamide (Schering Plough), Casodex (Zeneca) and Anandron$^{(R)}$ (Roussel)." See specification page 2, lines 2-8. Additionally, treatments to other diseases associated with androgen-dependent diseases, such as, for example, carcinoma of the prostate, common acne, hirsutism, early puberty, sexual deviations, androgenic alopecia, non-malignant prostatic hyperplasia or seborrhea, (see specification page 11, second paragraph) are also not objectively doubtable. Treatments to these diseases are known in the art. Even if this were not the case, there should be no enablement problem. See *Brana,* discussed later.

The Office Action nevertheless alleges that "there is a general lack of predictability in the pharmaceutical art," while citing *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970). However, there is no basis for such an allegation or conclusion. Fisher does not stand for the proposition that the pharmaceutical art is unpredictable *per se.* The court in Fisher stated that "in cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." Thus, merely concluding that the pharmaceutical art is unpredictable without looking at the factors involved is an improper basis for the allegation. As discussed in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988), used by the Examiner as the basis of the rejections, the court therein teaches that

"whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many **factual** considerations." No factual basis is provided by the Office Action for the conclusion that the art is unpredictable.

Additionally, with respect to *Fisher*, the court held therein that the appellant, who was the first to achieve a potency of greater than 1.0 for adrenocorticotrophic hormones ("ACTHs"), had not enabled the preparation of ACTHs having potencies much greater than 2.3, and the claim recitations of potency of "at least 1" rendered the claims insufficiently supported under the first paragraph of 35 U.S.C. §112. Thus, the situation and question considered by the court in *Fisher* is very different than the one present case. The applicant therein was the "first" to achieve a potency of greater than 1.0, but not greater than 2.3, while the claims were directed open endedly to a potency of "at least 1." In the present case, antiandrogens are already used in clinical practice to treat prostate cancer, and the claims are not open ended.

Even though compounds of similar activities are already known and clinically used in the art, the specification nevertheless provides guidance as to how the inhibitory action of the compounds can be determined. See, for example, example 119, directed to Antiproliferation Test with the Human Prostate Cancer Cell Line (LNCaP), where three of the prepared compounds were tested for activities. One of ordinary skill in the art through routine testing of the compounds, for example, as described in the specification, can determine the activity level of each synthesized compound of the claimed invention.

As discussed above, this is adequate to objectively enable an invention. Without proper reason or evidence to doubt the objective truth of the enabling disclosure, the Examiner improperly required a guarantee and/or evidence to prove utility and/or to support enablement. "Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility." *See In re Bundy*, supra.

With regard to *Wands*, the court therein further held that the "test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." Here, the compounds are enabled

and the rejection only concerns the method of use claims. Applicants provide specific guidance as to how the claimed compounds can be tested for activity levels. While the amount of work may require considerable effort (although not admitted), no undue experimentation is required in determining activity levels. In the pharmaceutical art testing hundreds and thousands of compounds, i.e., screening for activity, is merely routine. The allegation that determining biological activity for the claimed compounds is a "painstaking experimental study" is without factual basis, and even if true (not admitted to be), does not amount to "undue experimentation."

Instead of relying on proper probative evidence, the rejection is improperly based on bare allegations. No evidence has been presented which would demonstrate that the guidance provided by the specification is inadequate to enable the preparation and use of the claimed compounds without undue experimentation.

The Office Action also alleges that the results of the three tested compounds are "not enough data" to enable claims directed to the use of hundreds of compounds for use in "a broad range of disease states." Applicants submit that the three tested compounds are representative of the genus claimed. No factual basis to conclude otherwise is presented by the Office Action. The results of these studies establish that all three of the compounds have much better antiandrogeneity than OH-flutamide, and Casodex (both already used in clinical practice for prostate cancer treatment, see discussion above) and EM-101, a preferred compound of WO91/00732 directed to compounds that can act as inhibitors of androgen synthesis and/or as blockers of the androgen receptor (see specification page 2, last paragraph), while possessing no androgeneity, as do both flutamide, and Casodex in the tested experiments. See example 119, page 67 for results.

With respect to the variety of diseases claimed, the specification teaches that "androgen-dependent diseases are based on the reduction or as complete as possible elimination of androgen-induced effects. This can be done by blocking the domains of androgen receptor (AR), to which the androgens bind as ligands." See specification page 1, second paragraph. Thus, even though several diseases are associated with androgens, they are related by mode of action. The usefulness of a compound that inhibits the androgen receptor to treat an androgen-dependent disease is not objectively doubtable to a person of ordinary skill in the art.

With respect to pharmaceutical inventions, the specific issue of whether an applicant is required to test the claimed compounds in their final use has been also answered. The Federal

Circuit in *In re Brana*, supra, stated that

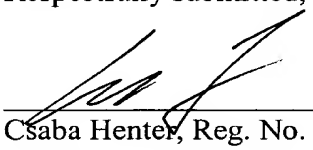
> usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful can be well before it is ready to be administered to humans. If the courts were to require Phase II testing in order to prove utility for pharmaceutical inventions, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Applicants also point to *In re Bundy*, 642 F.2d 430, 209 USPQ 48, (CCPA 1981), where the disclosure only established the basic pharmacology for the compounds, but where no examples were provided. The specification stated that the compounds of the invention possess activity similar to E-type prostaglandins. Nevertheless it was found that sufficient guidelines as to use were given in the disclosure. The court held that "what is necessary to satisfy the how-to-use requirement of section 112 is the disclosure of some activity coupled with knowledge as to the use of this activity."

Applicants provided adequate support and evidence to enable the method claims. Reconsideration is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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